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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,568	07/30/2001	Wataru Morikawa	20-48418	2810
2292	7590	03/01/2004	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			HARRIS, ALANA M	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 03/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/806,568	<b>Applicant(s)</b> MORIKAWA ET AL.	
	<b>Examiner</b> Alana M. Harris, Ph.D.	<b>Art Unit</b> 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 November 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 5-10, 13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 11 and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>6/28/01; 4/2/01</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. The Examiner of record has changed. Contact information is provided at the close of the action.

### ***Election/Restrictions***

2. Applicant's election with traverse of Group I (1, 11 and 12) in the Paper received November 6, 2003 is acknowledged. The traversal is on the ground(s) that the previous Examiner misinterpreted the claims and "[g]roups I-VI should be considered a single group since all...[refer] to the enzyme". This is found persuasive in part because the present Examiner is cognizant that SEQ ID NO: 1 refers to the enzyme and not the produced fragments and submits that it would not be burdensome to rejoined Groups I-V. However, because the technical feature shared between the remaining groups is not special the remainder of the Election/Restrictions requirement set forth and mailed October 6, 2003 is maintained.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-14 are pending.

Claims 5-10, 13 and 14, drawn to non-elected inventions are withdrawn from examination.

Claims 2, 4, 5, 9 and 11-14 have been amended.

Claims 1-4, 11 and 12 are examined on the merits.

### ***Claim Objections***

4. Claim 12 is objected to because of the following informality: Claim 12 does not further limit from claim 11. Essentially, the claimed subject matter is the same.

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for a method of treating lung cancer in a mouse, does not reasonably provide enablement for the said method for treating all cancers and preventing disease conditions merely associated with vascularization. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants have set forth evidence that when immunodeficient mice transplanted with Lewis lung cancer cells were treated with PACE4, inhibitory activity to the growth of the metastasized cancerous focus was observed in a dose dependent manner, see Example 11 on pages 48 and 49. However, the methodology listed in the specification

is not commensurate in scope with claims, particularly the method of broadly treating a solid cancer and prevention of broad disease conditions associated with vascularization. The term "solid cancer" reads on a number of cancers that have different histopathological features and infinite numbers of disorders can be attributed to the term "vascularization".

There is no guidance in the specification as to how to determine and select a population of individuals, which may or may not eventually have cancer. Preventing a disease is just as complex a process. It is not clear what parameters would one skilled in the art use in order to identify a population of subjects that cancer could be prevented. It is also not clear what symptoms one of skill in the art would need to identify before possibly treating a patient. While it is art known that clinicians are capable of implementing both screening and surveillance and the type of screening test used and the intervals at which it is performed are based on risk stratification, which also serves as the basis for selecting potential candidates for possible prevention. However, like most screening procedures determining whether a population will eventually be struck with a disease is not full proof.

There would also need to be some valid amount of direction or guidance, as well as presence or absence of working examples presented in the specification that would enable one skilled in the art to perform the method as presented in the recited claims. It appears that undue experimentation would be required of one skilled in the art to practice the instant claimed invention using the teachings of the specification. See Ex parte Forman, 230 USPQ 546 BPAI, 1986.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-4, 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 is vague and indefinite in the recitation "[a]n enzyme that produces plasma protein fragments having an inhibitor activity". It is not clear if the plasma protein fragments or the enzyme possesses the activity. For the purposes of examination the Examiner is interpreting the claim as the protein fragments having the activity. Notwithstanding, Applicants are requested to clarify.

b. Claim 2 is vague and indefinite in the recitation "having a high homology". It is not clear what is regarded as high and what type of homology is being assessed. For example, is the homology in question pertaining to the structure, amino acid sequence or pH level. The metes and bounds cannot be determined.

c. Claim 3 is vague and indefinite because it is not clear if the extracellular matrix proteins are mammalian or non-mammalian proteins.

d. Claim 11 is vague and indefinite in the recitation "solid cancer". It is not clear exactly what type of cancer Applicants are referencing. The metes and bounds of the claim cannot be determined.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Gately et al. (Cancer Research 56: 4887-4890, November 1, 1996/ IDS reference on sheet 1). Gately discloses a factor secreted by the PC-3 prostate carcinoma cell line that has enzymatic activity and is able to cleave plasminogen to bioactive angiostatin, see page 4887, abstract and introduction. This factor suppresses the growth of metastatic tumor cells, see introduction. The factor disclosed cleaves plasminogen and the resulting cleavage product's approximated mass is that of kringles 1-4 of human plasminogen, see page 4888, column 2, Angiostatin...section. Given the predicted mass of the plasminogen, it follows that the disclosed enzyme factor cleaves plasminogen at 73L-74F, as well as 451L-452P to produce fragments comprising Kringles 1 to 4 of plasminogen.

The PC-3 derived angiostatin was a potent inhibitor of *in vivo* angiogenesis in subjects with corneal angiogenesis, a disease condition associated with diabetic retinosis, see page 4889, bridging paragraph of columns 1 and 2. Furthermore, the administration of the enzymatic factor would not only treat corneal angiogenesis, but inherently confer treatment of a solid cancer, as well as rheumatism.

Although Gately does not specifically recite the molecular weight, the N-terminal amino acid sequence, SEQ ID NO: 1 and at what pH range the plasma protein fragments are degraded these limitations would be inherent qualities of the disclosed enzymatic factor in light of the fact it acts in the same manner as Applicants' claimed product.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



Art Unit: 1642

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.

PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Alana M. Harris', is written over the printed name.

Alana M. Harris, Ph.D.

2 February 2004